The Use of Proteomics in Diagnostics: Liver Fibrosis Biomarkers

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Proteomics can help to discover and quantify novel biomarkers and we show how this is achieved using liver fibrosis as an example. Liver biopsy is the reference standard for assessing liver fibrosis and serum biomarkers are less invasive. The severity of liver fibrosis can be determined using immunoassays. However biomarkers may be degraded due to sample storage conditions and therefore may not be detected using these antibody-based assays. Detection of biomarkers by mass spectrometry overcomes this disadvantage and the approach can be applied to all diseases.

Two dimensional gel electrophoresis (2DE) was used to find differences in proteins in plasma samples from patients with varying liver fibrosis stages. The identified proteins were potential liver fibrosis biomarkers. Mass spectrometry can assay for biomarkers by detecting their tryptic peptides and fragments and was used to develop an antibody-free assay. We are the first and only lab in the UK to use a novel absolute quantitation method which is the only biomarker assay using a universal calibration mix.

Using 2DE, we identified several potential biomarkers for liver fibrosis which were analysed by Western blotting using plasma samples from patients with varying stages of liver fibrosis. Our novel biomarkers were promising when compared to the markers used in current liver fibrosis tests. A mass spectrometry assay was developed for the best novel liver fibrosis biomarker.

We are working towards the first ever antibody-free biomarker assay for liver fibrosis. Our assay is nine times faster than conventional quantitation by mass spectrometry making our approach for absolute biomarker quantitation applicable for clinical use. This is also the only assay which can analyse all points of the calibration curve and determine the absolute concentration of the biomarker in a single acquisition. Our assay may help reduce the need for invasive liver biopsies and the approach could be used for any other disease.